

PEER REVIEWED

VITAL VACCINATION SERIES

ANTIBODY TITERS

versus

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The publication of vaccination guidelines for dogs and cats (see **Links to Vaccination Guidelines**, page 38)—intended to provide useful insights on the selection and use of vaccines—also elicited some degree of controversy regarding implementation of these vaccination recommendations in practice.

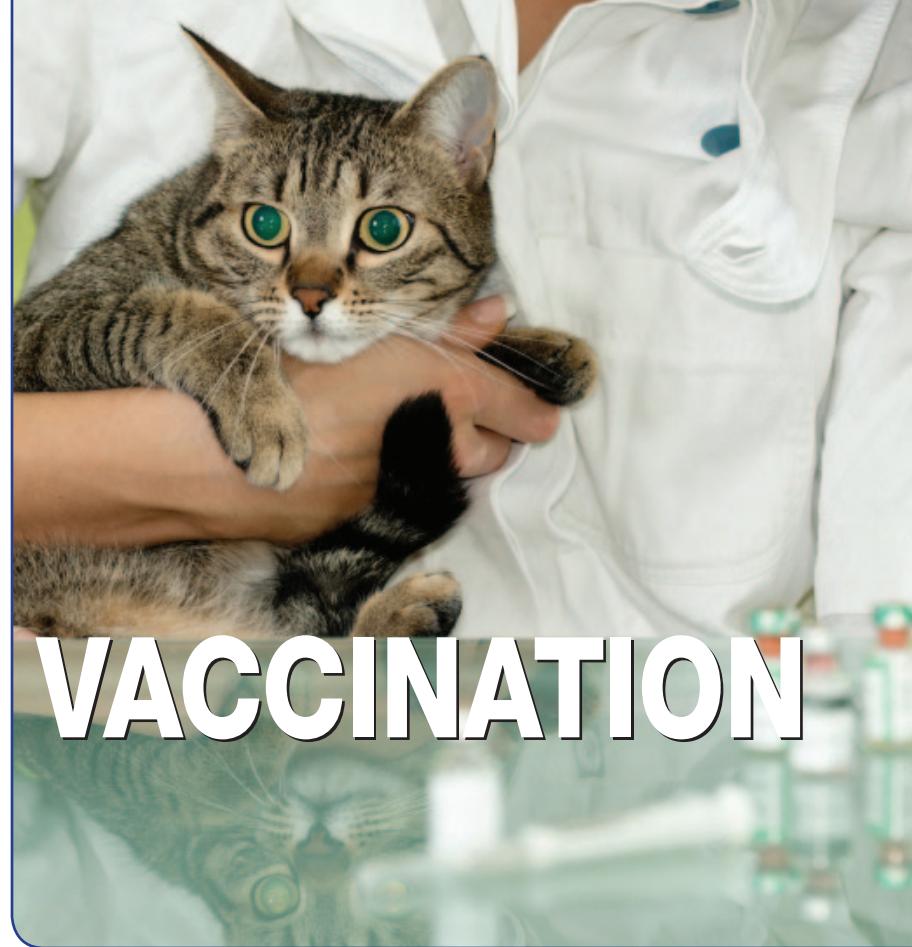
DURATION OF IMMUNITY CONCERNs

In particular, the recommendation to administer *core* vaccines to adult dogs and cats at 3-year intervals (or longer) rather than annually resulted in differences of opinion among veterinarians. After all, veterinarians have been recommending annual boosters for years, doing so in accordance with manufacturer recommendations.

Therefore, the growing group of veterinarians who were skeptical of triennial vaccination recommendations began measuring antibody titers from individual patients to assess duration of immunity (DOI) and determine whether a patient required revaccination. As demand for *vaccine titers* increased, veterinary laboratories began offering antibody titer panels for dogs and cats while 2 companies developed in-clinic antibody tests.

With the increased focus on antibody titers, additional questions were raised:

- What are the indications for performing titers?
- When interpreting antibody titers, what test limitations apply?
- How should test results be interpreted when making vaccination decisions for individual patients?



VACCINATION

CORRELATION OF TITERS & IMMUNITY

Antibody titers measured in laboratories and by in-clinic and antibody test kits typically record results as *positive* or *negative*, and include a brief description of the result's significance. However, questions remain:

- How well does a *positive* antibody titer (or test kit result) correlate with protective immunity in a patient?
- How well does a *negative* titer (or test kit result) correlate with susceptibility in a patient?

When interpreting antibody titers, a few facts must be clear:

1. **The only true test of protective immunity involves exposure (challenge) to a virulent pathogen** in which nonvaccinates (controls) are infected and manifest clinical illness while vaccinated animals remain healthy. Animal vaccines are licensed based on this premise.
2. **Interpreting antibody test results depends on understanding what results do and do not represent.** In the clinical setting, antibody levels offer diverse and distinct clinical applications (see **It's All About PIE**, page 36).
3. **Different classes of antibody, also called immunoglobulin (Ig), have specialized functions** (identified and categorized as IgA, IgG, IgE, or IgM). In veterinary medicine, the antibody titers used to assess protective immunity typically represent the IgG class.
4. When using an in-clinic test kit to measure (qualitative or semiquantitative) antibody levels, **results are reported as either positive (indicates protection) or negative (indicates susceptibility) and must be correlated with gold standard laboratory tests**, such as virus neutralization (VN) or hemagglutination inhibition (HI), in order

to accurately represent a defined threshold of antibody. Both in-clinic tests have been correlated through VN, HI, or challenge testing results. While the correlation studies were conducted independently through universities, the data is available through the respective companies that manufacture the in-clinic test kits.

Today, in-clinic titer test kits for canine distemper (CDV), canine parvovirus (CPV), canine adenovirus (CAV), and feline parvovirus (panleukopenia, FPV) correlate *well* with appropriate gold standard tests. Therefore, when these in-clinic tests are performed properly:

- A **positive** test result indicates the patient **does have protective levels** of antibody against the virus.
- A **negative** test result indicates the patient **does not have protective levels** of circulating antibody. However, a **negative** test result **does not necessarily define susceptibility**.

IT'S ALL ABOUT PIE

- **Protection (P):** Some, but not all, antibody results correlate well with protection (eg, canine and feline parvovirus). A patient with a positive titer or test result for parvovirus antibody can be considered protected.
- **Infection (I):** On the other hand, antibody presence can represent evidence of active infection (eg, feline immunodeficiency virus).
- **Exposure (E):** Other antibody test results indicate prior exposure to an infectious agent (eg, Ehrlichiosis) or vaccine (eg, rabies) and do not predict either protection or active infection.

ANTIBODY DEVELOPMENT LIMITATIONS

Seroconversion, the antibody response that follows vaccination, can be identified for most vaccines administered to dogs and cats. However, the development of antibody does not necessarily equate to **protective immunity**.

Feline Calicivirus & Herpesvirus

- Even if **antibody test results** are *positive* after feline herpesvirus (FHV) and feline calicivirus (FCV) vaccination, results *do not correlate well with protective immunity*; these results are not generally recommended for use when making vaccination decisions for an individual cat.
- The correlation between the **gold stan-**

dard antibody test for FHV-1 (VN) and protection is only *fair*; **cell-mediated immunity** is a *better correlate* of protection against FHV-1.

- The correlation between the **gold standard test** for FCV (VN) and protection is *fair to good*.

Rabies

Rabies antibody titers, as determined by **fluorescent antibody virus neutralization** (FAVN), are only available through a limited number of certified laboratories. It is important to note that a rabies virus antibody titer *cannot* be interpreted as an index of immunity in lieu of revaccination.

Factors that influence antibody response following vaccination include:

- Age
- Antigen type
- Vaccination history
- Health status
- Genetics
- Maternally-derived antibody (MDA)

INDICATIONS FOR ANTIBODY TESTING

The following indications apply to antibody tests for CAV-1, CDV, CPV, and FPV because these results correlate *well* with gold standard testing:

1. Evaluation of Immune Response Following Initial Administration of Core Vaccines

If a client would like to determine whether a young dog/cat responded to the initial vaccination series (usually 3 doses), in-clinic test kits provide an excellent means of identifying those that did respond versus those that did not and, therefore, remain susceptible.

2. Management of Infection Among Vaccinates

For veterinarians faced with treating confirmed parvovirus infection in a well vaccinated dog or cat, antibody testing can be used to rapidly determine whether the affected

TABLE 1. Tests to Determine Immunologic Protection

VIRUS	APPROPRIATE TESTS
Rabies	Rabies antibody titers are determined by FAVN. Test results cannot be used as an index of immunity in lieu of revaccination.
CANINE	
Adenovirus	In-clinic titer test results correlate <i>well</i> with gold standard testing (VN).
Distemper virus	In-clinic titer test results correlate <i>well</i> with gold standard testing (VN).
Parvovirus	In-clinic titer test results correlate <i>well</i> with gold standard testing (HI).
FELINE	
Calicivirus	The correlation between gold standard testing (VN) and protection is <i>fair to good</i> .
Herpesvirus	The correlation between gold standard testing (VN) and protection is <i>only fair</i> ; cell-mediated immunity is a <i>better correlate</i> of protection.
Parvovirus	In-clinic titer test results correlate <i>well</i> with gold standard testing (HI).

TABLE 2. In-Clinic Antibody Titer Test Kits

	TiterCHEK	VacciCheck Antibody Test Kit
Manufacturer	Synbiotics Corporation (synbiotics.com)	Biogal Galed Laboratories (biogal.co.il)
Canine Antibody	CDV and CPV	CAV, CDV, and CPV
Feline Antibody	None	FCV, FHV, and FPV
Sample	Serum or plasma (can use hemolyzed sample)	Serum, plasma, or whole blood (can use hemolyzed sample)
Test Time	15–20 min (minimum)	21 min (minimum)
Results	Qualitative: Positive or negative	Semiquantitative (based on color): Negative, low positive, significant positive, or high positive

animal developed a protective immune response following the initial vaccination series.

- A *positive antibody test* suggests the vaccinated patient was infected during a period of susceptibility (eg, in the presence of MDA).
- Patients with a *negative test result* are likely to be susceptible (genetic) non-responders (or low-responders).
- The antibody test *does not* distinguish vaccine-induced seroconversion from that caused by infection.

3. Determination of Antibody Level in Lieu of Revaccination

For patients with a history of a known, or suspected, serious vaccine adverse event (reaction), evaluating the level of antibody will determine whether the patient has previously developed a protective immune response to vaccination. Patients with a *positive test result* can avoid revaccination and potential risk for an adverse event.

If, on the other hand, a patient with a history of a serious vaccine adverse event is tested for antibody and has a *negative test result*, the decision whether or not to administer vaccine is more complicated because:

- Among previously vaccinated animals, immune *memory* (B-lymphocytes) can be sustained for many years despite declining antibody levels; exposure to a pathogenic virus (eg, distemper or parvovirus) can result in a rapid and protective anamnestic response.
- Prior history of a vaccine adverse reaction is not predictive of future risk.
- Immunization may not be optional, regardless of the antibody status of the individual (eg, rabies).

4. Assessment of Adult Dogs & Cats with an Unknown Vaccination History

Clientele who have adopted an adult dog/cat that has no known vaccine history may elect to avoid vaccination if a protective level of immunity can be determined serologically.

5. Antibody Testing in Lieu of Annual Revaccination

International guidelines for administration of core vaccines to adult dogs and cats consistently recommend revaccination schedules of no more *often* than every 3 years for core antigens (CAV-1*/CDV/CPV and FCV/FHV/FPV).

However, with regard to rabies vaccination, veterinarians must follow state or local laws.

6. Management of Infection Risk Among Animals Entering a Shelter

Immunization status of young animals presented to animal shelters is often unknown. Because the infection risk among shelter-housed dogs and cats is high, determining antibody status of an animal at time of entry allows vaccination and separation (foster) of animals deemed *susceptible* until a *positive* test result is obtained.

7. Management of Outbreaks Within an Animal Shelter

Antibody test kits offer shelters a management advantage when faced with an infectious disease outbreak involving CDV, CPV, or FPV. Identifying and separating animals with *positive* (protected) test results from those with *negative* (susceptible) results may help avoid unnecessary euthanasia.

When feasible, susceptible animals should be isolated from the general population, which limits propagation of the outbreak. Isolated, seronegative survivors can be placed or adopted once the incubation period for the infectious agent has passed (2 weeks for CPV and FPV; 6 weeks for CDV).

CORE VACCINE ADMINISTRATION & ANTIBODY TESTING

- Current vaccination guidelines recommend administration of the last dose of core vaccines at 14 to 16 weeks of age in puppies and 16 weeks of age in kittens.
- Antibody titers may be determined as early as 2 to 4 weeks following completion of initial vaccination series.
- A puppy or kitten that is *seronegative* at 18 weeks of age should be revaccinated not less than 2 weeks following the last dose. Antibody testing can then be performed as early as 2 weeks following administration of this last vaccine dose.

*All antibody tests detect antibodies against CAV-1; however, the vaccine antigen protects against CAV-2 (a respiratory pathogen), which also cross protects against the more serious, systemic CAV-1 (canine hepatitis virus).

LINKS TO VACCINATION GUIDELINES

- **2011 AAHA Canine Vaccination Guidelines:** aahonet.org/PublicDocuments/CanineVaccineGuidelines.pdf
- **2006 American Association of Feline Practitioners Feline Vaccine Advisory Panel Report:** catvets.com/uploads/PDF/2006VaccinationGuidelines_JAVMA.pdf
- **2010 WSAVA Guidelines for the Vaccination of Dogs and Cats:** wsava.org/sites/default/files/VaccinationGuidelines2010.pdf

INTERPRETATION OF ANTIBODY TEST RESULTS

The following interpretations apply to antibody test results for CAV-1*, CDV, CPV, and FPV, reported by a reputable diagnostic laboratory or obtained from an in-clinic test kit:

1. A **positive** antibody test result in an **unvaccinated, but healthy dog or cat** suggests prior exposure to and recovery from infection; the patient has **protective immunity**.
2. A **positive** antibody test result in a **previously vaccinated dog or cat** correlates well with **protective immunity**.
3. A **negative** antibody test result in a **previously vaccinated dog or cat** must be interpreted on the basis of age and prior vaccination history.
 - **Negative** test result in **protected patient**: Over time, antibody levels in a previously vaccinated adult dog or cat that is not revaccinated (or naturally exposed) may fall to **negative** levels. Memory cells (B-lymphocytes), however, can persist longer than antibody. Exposure to virulent virus is expected to rapidly boost the patient's antibody response and protect.
 - **Negative** test result in **susceptible patient**: A puppy or kitten that is antibody **negative** following administration of initial core vaccine series is considered **susceptible** to infection if exposed. These patients may be (genetic) non-responders (or low-responders) or received the vaccine during a period when interfering levels of MDA were present. ■

CAV = canine adenovirus; CDV = canine distemper; CPV = canine parvovirus; DOI = duration of immunity; FCV = feline calicivirus; FHV = feline herpesvirus; FAVN = fluorescent antibody virus neutralization; FPV = feline parvovirus (panleukopenia); HI = hemagglutination inhibition; Ig = immunoglobulin; MDA = maternally-derived antibody; VN = virus neutralization

Suggested Reading

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